AMENDMENTS TO THE CLAIMS

1–167. (Canceled)

168. (Currently amended) A method of identifying a molecular target for therapeutic intervention for a second trait in a second species, the method comprising:

(a) identifying a first gene in a segregating population that is causal for a first trait exhibited by all or a portion of said segregating population, wherein each member of said segregating population is a member of a first species and wherein said second trait in said second species corresponds to said first trait in said first species;

(b) mapping said first gene in said first species to a corresponding locus in the genome of the second species; and

(c) determining whether a marker or a haplotype in said corresponding locus in the genome of the second species associates with said second trait, wherein, when said marker or said haplotype associates with said second trait in said second species, said locus is identified as said molecular target for therapeutic intervention, wherein at least ~~one of steps (a), (b), and~~ step (c) is performed by a suitably programmed computer.

169. (Original) The method of claim 168 wherein said marker or said haplotype is in a second gene in said corresponding locus and said second gene is identified as said molecular target.

170. (Original) The method of claim 169 wherein said first gene and said second gene are orthologous.

LAW OFFICES OF
CHRISTENSEN O'CONNOR JOHNSON KINDNESS[PLLC]
1420 Fifth Avenue
Suite 2800
Seattle, Washington 98101
206.682.8100

171. (Original) The method of claim 168 wherein said identifying said first gene in said segregating population that is causal for said first trait exhibited by all or a portion of said segregating population comprises:

(a) identifying a test gene in said first species that has at least one abundance quantitative trait locus (eQTL) coincident with a respective clinical quantitative trait locus (cQTL) for said first trait; and

(b) testing, for one or more respective eQTL in said at least one eQTL, whether (i) the genetic variation of said eQTL across said segregating population and (ii) the variation of the first trait across said segregating population are correlated conditional on an abundance pattern of the test gene across said segregating population,

wherein, when the genetic variation of (1) said one or more respective eQTL tested in step (b) and (2) the variation of the first trait across said segregating population are correlated conditional on an abundance pattern of the test gene across said segregating population, said test gene is identified as said first gene.

172. (Original) The method of claim 168 wherein said second species is mammalian.

173. (Original) The method of claim 168 wherein said second species is human.

174. (Original) The method of claim 168 wherein said second trait is asthma, ataxia telangiectasia, bipolar disorder, cancer, common late-onset Alzheimer's disease, diabetes, heart disease, hereditary early-onset Alzheimer's disease, hereditary nonpolyposis colon cancer, hypertension, infection, maturity-onset diabetes of the young, mellitus, migraine, nonalcoholic fatty liver, nonalcoholic steatohepatitis, non-insulin-dependent diabetes mellitus, obesity, polycystic kidney disease, psoriases, schizophrenia, or xeroderma pigmentosum.

175. (Original) The method of claim 168 wherein said molecular target is a gene.

LAW OFFICES OF
CHRISTENSEN O'CONNOR JOHNSON KINDNESS PLLC
1420 Fifth Avenue
Suite 2800
Seattle, Washington 98101
206.682.8100

176. (Original) The method of claim 168 wherein said molecular target is an exon, an intron, or a regulatory element of a gene.

177. (Original) The method of claim 168 wherein said marker is a single nucleotide polymorphism, a microsatellite marker, a restriction fragment length polymorphism, a short tandem repeat, a DNA methylation marker, a sequence length polymorphism, a random amplified polymorphic DNA, an amplified fragment length polymorphisms, or a simple sequence repeat.

178. (Currently amended) A method of identifying a molecular target for therapeutic intervention for a second trait in a second species, the method comprising:

(a) identifying a first gene in a segregating population that is causal for a first trait exhibited by all or a portion of said segregating population, wherein each member of said segregating population is a member of a first species and wherein said second trait in said second species corresponds to said first trait in said first species;

(b) identifying a locus in the genome of the second species that is (1) linked to said second trait and (2) maps to the position in the genome of said first species where said first gene resides; and

(c) determining whether a marker or a haplotype in said corresponding locus in the genome of the second species associates with said second trait, wherein, when said marker or said haplotype associates with said second trait in said second species, said locus is identified as said molecular target for therapeutic intervention, wherein at least ~~one of steps (a), (b), and~~ step (c) is performed by a suitably programmed computer.

LAW OFFICES OF
CHRISTENSEN O'CONNOR JOHNSON KINDNESS PLLC
1420 Fifth Avenue
Suite 2800
Seattle, Washington 98101
206.682.8100

179. (Original) The method of claim 178 wherein said marker or said haplotype is in a second gene in said corresponding locus and said second gene is identified as said molecular target.

180. (Original) The method of claim 179 wherein said first gene and said second gene are orthologous.

181. (Original) The method of claim 178 wherein said identifying said first gene in said segregating population that is causal for said first trait exhibited by all or a portion of said segregating population comprises:

(a) identifying a test gene in said first species that has at least one abundance quantitative trait locus (eQTL) coincident with a respective clinical quantitative trait locus (cQTL) for said first trait; and

(b) testing, for one or more respective eQTL in said at least one eQTL, whether (i) the genetic variation of said eQTL across said segregating population and (ii) the variation of the first trait across said segregating population are correlated conditional on an abundance pattern of the test gene across said segregating population,

wherein, when the genetic variation of (1) said one or more respective eQTL tested in step (a) and (2) the variation of the first trait across said segregating population are correlated conditional on an abundance pattern of the test gene across said segregating population, said test gene is identified as said first gene.

182. (Original) The method of claim 178 wherein said second species is mammalian.

183. (Original) The method of claim 178 wherein said second species is human.

LAW OFFICES OF
CHRISTENSEN O'CONNOR JOHNSON KINDNESS PLLC
1420 Fifth Avenue
Suite 2800
Seattle, Washington 98101
206.682.8100

184. (Original) The method of claim 178 wherein said second trait is asthma, ataxia telangiectasia, bipolar disorder, cancer, common late-onset Alzheimer's disease, diabetes, heart disease, hereditary early-onset Alzheimer's disease, hereditary nonpolyposis colon cancer, hypertension, infection, maturity-onset diabetes of the young, mellitus, migraine, nonalcoholic fatty liver, nonalcoholic steatohepatitis, non-insulin-dependent diabetes mellitus, obesity, polycystic kidney disease, psoriases, schizophrenia, or xeroderma pigmentosum.

185. (Original) The method of claim 178 wherein said molecular target is a gene.

186. (Original) The method of claim 178 wherein said molecular target is an exon, an intron, or a regulatory element of a gene.

187. (Original) The method of claim 178 wherein said marker is a single nucleotide polymorphism, a microsatellite marker, a restriction fragment length polymorphism, a short tandem repeat, a DNA methylation marker, a sequence length polymorphism, a random amplified polymorphic DNA, an amplified fragment length polymorphisms, or a simple sequence repeat.

188. (Currently amended) A method of identifying a molecular target for therapeutic intervention for a second trait in a second species, the method comprising:

(a) identifying a first gene in a segregating population that is causal for a first trait exhibited by all or a portion of said segregating population, wherein each member of said segregating population is a member of a first species and wherein said second trait in said second species corresponds to said first trait in said first species; and

(b) identifying a second gene in the genome of the second species that is orthologous to said first gene and in which (i) the variation of the abundance of the second gene across biological samples taken from a plurality of members of said second species and (ii) the

LAW OFFICES OF
CHRISTENSEN O'CONNOR JOHNSON KINDNESS PLLC
1420 Fifth Avenue
Suite 2800
Seattle, Washington 98101
206.682.8100

variation of the second trait across said plurality of members of said second species are associated, wherein said second gene is identified as said molecular target for therapeutic intervention, and wherein at least ~~one of steps (a) and~~ step (b) is performed by a suitably programmed computer.

189. (Original) The method of claim 188, the method further comprising: validating said second gene by determining whether a marker or a haplotype in said second gene associates with said second trait, wherein, when said marker or said haplotype associates with said second trait in said second species, said second gene is validated.

190. (Original) The method of claim 188 wherein said identifying said first gene in a segregating population that is causal for a first trait exhibited by all or a portion of said segregating population comprises:

(a) identifying a test gene in said first species that has at least one abundance quantitative trait locus (eQTL) coincident with a respective clinical quantitative trait locus (cQTL) for said first trait; and

(b) testing, for one or more respective eQTL in said at least one eQTL, whether (i) the genetic variation of said eQTL across said segregating population and (ii) the variation of the first trait across said segregating population are correlated conditional on an abundance pattern of the test gene across said segregating population,

wherein, when the genetic variation of (1) said one or more respective eQTL tested in step (b) and (2) the variation of the first trait across said segregating population are correlated conditional on an abundance pattern of the test gene across said segregating population, said test gene is identified as said first gene.

191. (Original) The method of claim 188 wherein said second species is mammalian.

LAW OFFICES OF
CHRISTENSEN O'CONNOR JOHNSON KINDNESS PLLC
1420 Fifth Avenue
Suite 2800
Seattle, Washington 98101
206.682.8100

192. (Original) The method of claim 188 wherein said second species is human.

193. (Original) The method of claim 188 wherein said second trait is asthma, ataxia telangiectasia, bipolar disorder, cancer, common late-onset Alzheimer's disease, diabetes, heart disease, hereditary early-onset Alzheimer's disease, hereditary nonpolyposis colon cancer, hypertension, infection, maturity-onset diabetes of the young, mellitus, migraine, nonalcoholic fatty liver, nonalcoholic steatohepatitis, non-insulin-dependent diabetes mellitus, obesity, polycystic kidney disease, psoriases, schizophrenia, or xeroderma pigmentosum.

194. (Original) The method of claim 188 wherein said marker is a single nucleotide polymorphism, a microsatellite marker, a restriction fragment length polymorphism, a short tandem repeat, a DNA methylation marker, a sequence length polymorphism, a random amplified polymorphic DNA, an amplified fragment length polymorphisms, or a simple sequence repeat.

195–202. (Canceled)

LAW OFFICES OF
CHRISTENSEN O'CONNOR JOHNSON KINDNESS[PLLC]
1420 Fifth Avenue
Suite 2800
Seattle, Washington 98101
206.682.8100